## Phenylketonuria (PKU) (mRNA-3283)

**Last program update: May 6, 2021**

<table>
<thead>
<tr>
<th>Modality</th>
<th>ID #</th>
<th>Program Indication</th>
<th>Preclinical development</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3 and commercial</th>
<th>Moderna rights</th>
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<tr>
<td>Systemic intracellular therapeutics</td>
<td>mRNA-3927</td>
<td>PCCA/PCCB Propionic acidemia, PA</td>
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<tr>
<td></td>
<td>mRNA-3705</td>
<td>MUT Methylmalonic acidemia, MMA</td>
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<tr>
<td></td>
<td>mRNA-3283</td>
<td>PAH Phenylketonuria, PKU</td>
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<td>mRNA-3745</td>
<td>G6Pase Glycogen storage disease type 1a, GSD1a</td>
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**mRNA-3283 is in IND-enabling GLP toxicology studies**
Phenylketonuria (PKU) overview

Opportunity to address unmet need

- PKU is a rare inherited metabolic disease resulting from a deficiency in the metabolism of phenylalanine, or PHE, due to mutations within the enzyme phenylalanine hydroxylase, PAH.

- **Disease burden:** Progressive mental disability from tyrosine deprivation.

- **Target population:** Incidence of ~1:10K-15K live births in the US
  - ~21,000-32,000 patients in the US.

- **Approved therapies include:**
  - 20-56% of patients respond favorably to BioMarin’s Kuvan.
  - Non-responsive patients treated with restricted diet.
  - Biomarin’s Palynziq was approved in May 2018.

**Moderna concept:** IV-administered mRNA encoding PAH enzyme to restore deficient or defective intracellular enzyme activity.
Phenylketonuria (PKU) (mRNA-3283)

Preclinical data – restoration of enzymatic activity

Study Design:
- **Species:** Mouse
- **Animals:** PAH-/-
- **Dose:** 0.5 mpk
- **Dosing Schedule:** weekly
- **Injection Route:** IV
- **Sample Size:** [5-6]

PHE reduction with repeat dosing of PAH mRNA

*We have demonstrated the ability to impact PHE levels with repeat dosing of our mRNA in pre-clinical studies*

*Data not collected due to a snow storm*
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